REMARKS

Obviousness-Type Double Patenting Rejections

Applicants will attend to these provisional rejections after allowable matter has been identified.

Regarding US 11/887,268, which is a later filed pending application, MPEP 804(I)(B)(1) states that

> If a "provisional" nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer.

Accordingly, the withdrawal of this rejection is respectfully requested if and when said application will be still pending when the present application is allowed.

The Rejections Under 35 USC § 112, first paragraph

The Office Action rejects product claims, i.e., compound claims, which compounds in the application are disclosed to have pharmaceutical activity by inhibiting histone deacetylases. In sum, the rejection of these product claims is set forth as if the claims were method claims for use as inhibitors of enzymes generally, i.e., the specific enzyme discussed in the application is not even mentioned in the rejections. While the specification discloses inhibition of histone deacetylases (HDACs) as a possible use in the specification, the claims rejected nowhere require or recite a use. As such, the rejections are improper.

Very informative to whether the rejections are proper under controlling precedents is the decision of the Federal Circuit, holding specifically that a composition claim cannot be read to embrace only certain uses because the composition claim would otherwise mutate into a method claim. See *Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 54 USPQ2d 1227 (Fed. Cir. 2000), wherein the Federal Circuit stated that "the '393 patent **claims compositions of matter. The scope of these composition claims cannot ... embrace only certain uses of that composition. ... Otherwise these composition claims would mutate into method claims**."

Also important to note is the analysis used by the Federal Circuit in determining whether a pharmaceutical composition was enabled in *Amgen Inc. v. Hoechst Marion Roussel*

Inc., 65 USPQ2d 1385 (Fed. Cir. 2003). The inquiry exclusively focused on whether the individual components of a pharmaceutical composition were enabled and not on whether a particular use of said composition would be enabled. See the relevant part of the *Amgen* decision, which is reproduced below.

> Focusing specifically on the '422 patent, **the enablement inquiry** is whether Amgen has enabled all **pharmaceutical compositions** comprising "a therapeutically effective amount of human erythropoietin," "a pharmaceutically acceptable diluent, adjuvant or carrier," and human erythropoietin "purified from mammalian cells grown in culture." The court found that the specification described and enabled various possible diluents and carriers and provided specific information on effective dosages and therapeutic effect in mice. Id. at 148, 57 USPQ2d at 1506. Amgen also described and enabled at least one way of obtaining EPO purified from mammalian cells in culture: the genetic manipulation of CHO and COS-1 cells, followed by both described and other well known purification techniques. Finally, the court accepted testimony indicating that an ordinarily skilled artisan would infer from the COS-1 (monkey) and CHO cell examples that similar outcomes could be expected from other mammalian cells since all mammalian cells produce and secrete hormones like EPO by means of the same fundamental processes. Id. at 159, 57 USPQ2d at 1514-15. (Emphasis added.)

There is no basis for treating a product claim as if it was a method claim directed to particular use(s) in view of controlling precedents.

As such, even for the above reasons, the rejection cannot be maintained. Nevertheless, applicants provide the following.

MPEP 2164.01(c) may be of further guidance in this matter. This section teaches that "when a compound or composition claim is not limited by a recited use [which is the case here], any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use." Thus, any enabled use should preclude a rejection. No allegation whatsoever is made, and certainly not supported by facts or evidence, in the Office Action alleging that all disclosed uses lack enablement. Merely a broad allegation is made that inhibiting enzymes is unpredictable, and the alleged lack enablement followed. As such, the rejection should be precluded in view of this section of the MPEP.

The apparent main basis of the rejection in the Office Action is the allegation that enzyme inhibition is unpredictable. See, e.g., at the bottom of page 5 alleging the „highly unpredictable nature of inhibiting enzymes" at the bottom of page 6 alleging that „inhibiting enzymes is a very unpredictable art," while citing *Kubinyi*, and in the middle of page 7 alleging that „inhibiting enzymes is highly unpredictable" while again referencing *Kubinyi*. *Kubinyi* is a paper dealing with designing inhibitors generally. Nothing regarding the particular art or enzyme at issue in the present case is discussed at all. Nor is there a discussion of a class of compounds for the inhibition of any enzyme. Merely generic considerations in inhibitor design are discussed very generically. As such, this reference is completely irrelevant even if method claims were at issue in the present case.

Applicants bring the attention of the Examiner to the herewith submitted reference, i.e., *Miller et al.*, Histone Deacetylase Inhibitors, Journal of Medical Chemistry, Vol. 46, No. 24, 2003, 5097-5116. This overview article teaches on the first page thereof that "a wide range of structures have been shown to inhibit the activity of class I/II HDAC enzymes" and that they include among others "small-molecule hydroxamates, carboxylates, benzamides, electrophilic ketones, and cyclic peptides." Also discussed are the advances in design of such inhibitors in the recent years, which led to "an expansive group of agents that target class I/II HDACs." Throughout the reference a very large number of reported HDAC inhibitors are discussed and even illustrated by structure, demonstrating the expansive variety of structures being known to have the inhibiting activity involved in the present application. Also of importance is the large amount of HDAC related art discussed in especially the first four pages of the application, discussing clinical studies, relationship of such activity to a variety of diseases, e.g., cancer, etc. Such evidence are certainly much more relevant than *Kubinyi* cited by the Office Action, which does not even mention HDACs.

As the Examiner knows, even if the rejections were over method claims, which they are not, the standard for carrying the burden of establishing a lack of enablement has not been met herein. In a proper enablement rejection, first and foremost, a specification disclosure which "contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Marzocchi*, 169

U.S.P.Q. 367, 369 (1971). "The PTO must have adequate support for its challenge to the credibility of applicant's statements of utility". (The quoted statement was made in the context of enablement, i.e., the how-to-use requirement of the first paragraph of section 112.) See also *In re Bundy*, 209 USPQ 48 (1981). The only relevant concern of the Patent Office should be over the truth of assertions relating to enablement. The first paragraph of section 112 requires nothing more than objective enablement. See *In re Marzocchi, supra.*

The Examiner has not established any basis to doubt objective enablement. The Examiner has also provided no support for establishing that one of ordinary skill would doubt the objective truth of the asserted utility, which is enabled by the specification. Merely a broad allegation is made that enzyme inhibition in general is unpredictable, which is inadequate, especially in view of the disclosure in the application along with data on numerous exemplified compounds, and in further view of the state of the art as demonstrated by the herewith submitted reference by *Miller et al.* The enablement rejections by the Examiner are thus unfounded. The rejection therefore was improper under *In re Marzocchi.*

Even if the rejected claims would be directed to methods of inhibition, or methods of treatment, in view of what was known in the art, e.g., even Miller at al. on the first page teaching that HDAC enzymes are an emerging therapeutic target for the treatment of cancer and other diseases, that these agents are effective inhibitors of tumor growth, there is no basis for the rejections. The treatments and inhibitions recited above are not objectively doubtable. There is no indication that one of ordinary skill in the art would have questioned the effect of the drugs in view of the disclosure and the state of the art. See *Rasmusson v. Smithkline Beecham Co.*, 75 USPQ2d 1297 (Fed. Cir. 2005).

The Office Action also cites *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) when alleging that the scope of enablement varies inversely with the degree of unpredictability of the factors involved. However, the degree of unpredictability in this art is not as alleged, but rather as depicted by the specification and by the herewith provided reference demonstrating that one of ordinary skill in the art knows that a variety of compounds are HDAC inhibitors, that rational design tools are available and have already led to an expansive group of agents having said activity.

Additionally, with respect to *Fisher*, the court held therein that the appellant, who was the first to achieve a potency of greater than 1.0 for adrenocorticotrophic hormones ("ACTHs"), had not enabled the preparation of ACTHs having potencies much greater than

2.3, and the claim recitations of potency of "at least 1" rendered the claims insufficiently supported under the first paragraph of 35 U.S.C. §112. Thus, the situation and question considered by the court in *Fisher* is very different than the one present case. The applicant therein was the "first" to achieve a potency of greater than 1.0, but not greater than 2.3, while the claims were directed with an open end to a potency of "at least 1." In the present case, other compounds are already known to treat conditions associated with HDAC activity, and the claims are not open ended.

Applicants also disagree with the allegation that the ranges of activities provided for the exemplified compounds in the biological examples provide substantial uncertainty. The data clearly demonstrate that the compounds recited have the activity as taught in the application.

Applicants provided adequate support and evidence to enable the method claims. Reconsideration is respectfully requested.

Withdrawn Claims

Applicants remind the Examiner of 37 CFR 1.141, according to which an applicant is entitled to consideration of claims to additional species which are written in independent form or otherwise include all the limitations of an allowed generic claim. Because no prior art was found against the claims, there is no basis for not examaning the species, for example, within the scope of withdrawn dependent product claims 8-11.

Also, once the examined claims are found allowable, applicants request that in accord with the rejoinder provisions of the MPEP, at least the method claims be rejoined and examined in this application.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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